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Original article

High-sensitivity troponin T is a prognostic marker for patients with aortic stenosis after valve replacement surgery

Toshinobu Saito (MD), Yukihiro Hojo (MD, PhD)*, Masahiro Hirose (MD), Tomokazu Ikemoto (MD), Takaaki Katsuki (MD, PhD), Kazuomi Kario (MD, PhD, FJCC)

Department of Cardiology, Jichi Medical University, 3311 Yakushiji, Shimotsuke-city, Tochigi 329-0498, Japan

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ABSTRACT

Background: Aortic stenosis (AS) is recognized as a cause of sudden cardiac death. Recently, the measurement of high-sensitivity troponin T (hs-TnT) has become possible. Several studies have clarified that hs-TnT is a marker to indicate mortality of cardiovascular diseases.
Objectives: To examine whether hs-TnT can be used as a prognostic marker to predict the operative outcome of AS.
Methods: We enrolled 60 patients with AS (mean age = 68.7 ± 9.6 years, male/female = 30/30). Cardiac catheterization and echocardiography were performed to evaluate the severity of AS. Aortic valve replacement surgery was performed in all patients. We defined major adverse cardiac events (MACE) as composite events of heart failure, fatal arrhythmia, and all causes of death.
Results: We followed up the patients for 922 ± 800 days. Mean left ventricular ejection fraction was 60.0 ± 1.8%. Mean aortic valve area was 0.61 ± 0.03 cm^2. MACE occurred in 11 patients (18%), including 5 sudden cardiac deaths. We divided the patients into three groups based on the percentile of the plasma levels of hs-TnT. Kaplan–Meier curve revealed a statistically significant difference in MACE rate among the groups (log-rank test, $\chi^2 = 13.0$, $p = 0.002$). We conducted a Cox proportional hazard analysis with a model including age, sex, estimated glomerular filtration rate, and hs-TnT tertile as explanatory variables to predict MACE. We found that hs-TnT tertile to be a significant factor to predict MACE (hazard ratio: 3.71, $p = 0.03$).
Conclusions: hs-TnT can be a prognostic marker for patients with AS after valve replacement surgery.

Introduction

Aortic stenosis (AS) is associated with a poor prognosis once symptoms ensue [1,2]. Commonly, a decision on aortic valve replacement for severe AS is based on symptoms such as angina, syncope, and heart failure. However, there is marked mismatch between the onset of symptoms and severity of valvular stenosis. It makes it difficult to decide optimal operative time and predict prognosis of AS patients. Therefore, the establishment of a simple and objective marker to predict the prognosis of this disorder is needed.

Aortic valve replacement (AVR) is the standard treatment for severe AS, alleviating symptoms and improving survival [3–5]. However, despite the recent development of AVR, critical cardiovascular events such as fatal arrhythmias and congestive heart failure (CHF) remain problematic. The prognosis of patients with AS who have undergone AVR has improved, but a number of major adverse cardiovascular events (MACE) especially cardiac sudden death occur even after AVR. Therefore, the detection and management of high-risk patients have potential importance.

Cardiac troponins are ideal biochemical markers for the detection of myocardial cell injury because of their high-sensitivity and specificity, especially as markers of acute coronary syndrome [6–10]. Minute elevations of cardiac troponin are reported to be related to cardiovascular risk factors, carotid artery plaque burden, and myocardial dysfunction [11]. Previously, undetectable cardiac troponin T concentrations have been documented to contain substantial diagnostic and prognostic information [12–14]. Recently, a new high-sensitivity cardiac troponin T (hs-TnT) assay that can detect low levels of circulating cardiac troponin T has emerged. The new method makes it possible to measure concentrations >10-fold lower than the lower limit of the traditional assay. The superior sensitivity of the new assay currently provides a method that can detect cardiac troponin T levels in most patients with stable [15] and subclinical cardiovascular disease [16].

* Corresponding author at: Department of Cardiology, Jichi Medical University, 3311 Yakushiji, Shimotsuke-city, Tochigi 329-0498, Japan. Tel.: +81 285 58 7344; fax: +81 285 44 5317.
E-mail address: yhojo@jichi.ac.jp (Y. Hojo).

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We hypothesized that preoperative plasma hs-TnT is related to cardiovascular events in patient with severe AS who have undergone AVR. In this study, we have measured plasma levels of hs-TnT and investigated their clinical significance in patients with AS.

Subjects and methods

Patients

Consecutive patients who underwent AVR for the treatment of severe AS in Jichi Medical University Hospital between July 2003 and October 2010 were included in this study. Before AVR, all patients were subjected to cardiac catheterization and echocardiography to estimate the left ventricular ejection fraction (LVEF), aortic valve area (AVA), and pressure gradient (PG) between the left ventricle and aorta. We confirmed whether they had coronary artery disease, aortic regurgitation, and mitral regurgitation by cardiac catheterization and echocardiography.

Prosthetic valves were implanted into the aortic valve according to the operators' decision. After the AVR, all patients were followed up regularly every 4–8 weeks. The primary endpoint was the occurrence of MACE defined as composite events of re-admission to the hospital for CHF, fatal arrhythmia, and all causes of death. Fatal arrhythmia included ventricular tachycardia, ventricular fibrillation, and complete atrioventricular block.

We excluded patients with coronary artery disease, acute coronary syndrome, severe aortic regurgitation, combined mitral valvular disease, acute renal failure, and inoperable patients. Coronary artery disease was defined as evidence of significant stenosis of the epicardial coronary artery on angiograms (over 75% stenosis in the artery and over 50% stenosis in left main trunk). LVEF was measured by a modified Simpson's method and left ventricular mass and relative wall thickness by standard formulas by echocardiography. High-sensitivity C-reactive protein (hs-CRP) was measured by latex nephelometry as described by Ledue et al. [17]. Other biochemical substances were determined by standard assays. Hypertension [18], dyslipidemia [19], and diabetes mellitus [20] were diagnosed according to the criteria described by guidelines for each disease. The Ethics Committee of Jichi Medical University approved the study protocol. All patients enrolled in this study provided informed consent.

Measurement of plasma high-sensitivity troponin T levels

Peripheral blood was taken from the patients before cardiac catheterization. Anti-coagulated samples were then centrifuged immediately at $1000 \times g$ (4 °C, 15 min) and stored at −80 °C until the assay. The concentration of hs-TnT in plasma was determined using electrochemiluminescence immunoassay kits according to the manufacturer's instructions (Roche Diagnostics GmbH, Mannheim, Germany). The test has an analytic range of 0.003–10 ng/mL, and the 99th percentile cutoff point has been reported as ≥0.014 ng/mL in healthy individuals [21].

Statistical analysis

All values are expressed as the mean ± SEM unless otherwise indicated. The significance of differences between the three groups was determined by a one-way analysis of variance for the parametric analysis and the Kruskal–Wallis test for the non-parametric analysis. The change in hemodynamic data before and after the operation was analyzed using Student's paired t test. Categorical variables were expressed as percentages and analyzed using the χ-square test or Fisher's exact test. Kaplan–Meier survival curve and Cox proportional hazard model analyses were conducted with computer software (SPSS version 16.0, Chicago, IL, USA). Values of $p < 0.05$ were considered significant.

Results

Basic characteristics of study subjects

We studied 60 patients (aged 68.7 ± 9.6 years), of whom 30 (50%) were male. The number of patients with chest pain, syncope, and heart failure was 28 (46.7%), 11 (18.3%), and 23 (38.3%), respectively. Table 1 shows the baseline characteristics of the subjects. The mean plasma hs-TnT level was higher than that in normal individuals (≥0.014 ng/mL).

In cardiac catheterization, the average catheter-derived peak-to-peak PG through the aortic valve, left ventricular end-diastolic volume index (LVEDVI), and left ventricular end-systolic volume index (LVESVI) were 77.4 ± 4.0 mmHg, 98.0 ± 5.3 mL/m^2, and 41.4 ± 4.0 mL/m^2, respectively. The left ventricular end-diastolic pressure and pulmonary capillary wedge pressure were 22.2 ± 1.04 mmHg and 11.9 ± 0.78 mmHg, respectively. Cardiac index was 3.09 ± 0.09 L/min/m^2. The comparison of echocardiographic findings (pre-operation and before discharge) revealed that the peak PG, mean systolic PG, and left ventricular mass index decreased significantly (from 96.2 ± 3.0 mmHg to 32.4 ± 1.4 mmHg, $p < 0.001$, from 58.8 ± 2.3 mmHg to 18.5 ± 1.1 mmHg, $p < 0.001$, and from 177.9 ± 8.3 g/m^2 to 160.5 ± 9.6 g/m^2, $p < 0.05$, respectively) with AVR. The left ventricular end-diastolic diameter reduced significantly (from 47.6 ± 0.99 mm to 43.5 ± 0.80 mm, $p < 0.001$), while interventricular septal thickness (IVST) and posterior wall thickness (PWT) did not change significantly (IVST: from 14.2 ± 0.34 mm to 14.1 ± 0.28 mm, $p = 0.79$; PWT: from 13.6 ± 0.28 mm to 13.3 ± 0.24 mm, $p = 0.28$). AVA increased significantly (from 0.61 ± 0.03 cm^2 to 1.13 ± 0.06 cm^2, $p < 0.001$) after the operation. LVEF did not change significantly (from 60.0 ± 1.8% to 62.3 ± 1.6%, $p = 0.18$).

In operative findings, bicuspid aortic valves were found in 34 patients (56.7%) and atherosclerotic changes in the remaining 26 patients (43.3%). Twenty-six (43.3%) patients received a mechanical prosthetic and 34 patients, a bioprosthetic valve replacement according to the operator's decision. Six (10%) patients underwent

Table 1
Baseline characteristics of the subjects.

Age (mean ± SD, years)	68.7 ± 9.6
Male patients (%)	30 (50)
Body mass index (kg/m^2)	23.2 ± 0.5
Hypertension (%)	40 (66.7)
Dyslipidemia (%)	18 (30.0)
Diabetes mellitus (%)	17 (28.3)
Smoking (%)	9 (15.0)
The peak-to-peak PG (mmHg)	77.4 ± 4.0
LVEDVI (mL/m^2)	98.0 ± 5.3
LVESVI (mL/m^2)	41.4 ± 4.0
LVEF (%)	60.0 ± 1.8
Aortic valve area (cm^2)	0.61 ± 0.03
The maximum PG (mmHg)	96.2 ± 3.0
The mean PG (mmHg)	58.8 ± 2.3
LVMI (g/m^2)	177.9 ± 8.3
hs-CRP (ng/mL)	2216 ± 686
eGFR (mL/min/1.73 m^2)	67.6 ± 3.1
hs-TnT (ng/mL)	0.110 ± 0.088

SD, standard deviation; PG, pressure gradient through aortic valve; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; hs-TnT, high-sensitivity troponin T. The peak-to-peak PG, LVEDVI, and LVESVI were measured by cardiac catheterization. LVEF, aortic valve area, the maximum PG, the mean PG, and LVMI were measured by echocardiography.

graft replacement of the ascending aorta and one (1.7%) patient received tricuspid annuloplasty, concurrently.

Fig. 1 shows the distribution of plasma hs-TnT in our study population. Mean plasma hs-TnT was 0.110 ng/mL with standard deviation of 0.682 ng/mL and standard error of 0.088 ng/mL. Maximum and minimum values were 0.003 ng/mL and 5.30 ng/mL, respectively. Median value of hs-TnT was 0.015 ng/mL. We did not find significant correlation between plasma levels of hs-TnT and echocardiographic parameters associated with AS (mean systolic PG through the aortic valve, AVA, IVST, PWT, and left ventricular dimensions). As shown in Table 2, we found significant correlations between plasma hs-TnT and clinical parameters, age, aspartate aminotransferase, hs-CRP, estimated glomerular filtration rate (eGFR), and N-terminal pro-B-type natriuretic peptide (NT-pro BNP). We performed multiple regression analysis using hs-TnT as a responsive variable and age, aspartate aminotransferase, hs-CRP, eGFR, and NT-pro BNP as explanatory variables. We found that NT-proBNP was a significant variable for plasma hs-TnT ($\beta = +0.67$; $p < 0.001$).

High-sensitivity troponin T levels as a predictor of MACE

We examined whether plasma levels of hs-TnT can be used to predict MACE after AVR. The mean follow-up period was 922 ± 800 (14–2300) days. MACE occurred in 11 patients (18.3%). We divided the patients into three groups based on the percentile of the plasma hs-TnT level: 0.003 to <0.011 ng/mL (T1: first tertile, $n = 16$), 0.011 to <0.0237 ng/mL (T2: second tertile, $n = 24$), and 0.0237 to <5.3 ng/mL (T3: third tertile, $n = 20$). The mean level of hs-TnT in T1, T2, and T3 was 0.007 ± 0.001 ng/mL, 0.015 ± 0.001 ng/mL, and 0.306 ± 0.263 ng/mL, respectively. Table 3 shows the baseline clinical characteristics of the subjects in the groups and the patients divided by hs-TnT tertiles, respectively. The incidence of heart failure in T2 and T3 was significantly higher compared with that in T1 before the operation. The eGFR was significantly lower in T3 than that in T1. As shown in Fig. 2, Kaplan–Meier curves revealed a statistically significant difference in the occurrence of MACE among the three groups (log-rank test, $\chi^2 = 13.0$, $p = 0.002$). Post hoc analysis revealed that the incidence of MACE was significantly different between T1 and T3 ($p = 0.01$) and T2 and T3 ($p = 0.01$). We summarized the cardiovascular events in the three groups (Table 4). When we divided patients into two groups according to the normal value of plasma hs-TnT (<0.014 mg/mL or ≥0.014 ng/mL), Kaplan–Meier curve analysis revealed a statistically significant difference in the occurrence of MACE between the two groups (log-rank test, $\chi^2 = 6.24$, $p = 0.04$).

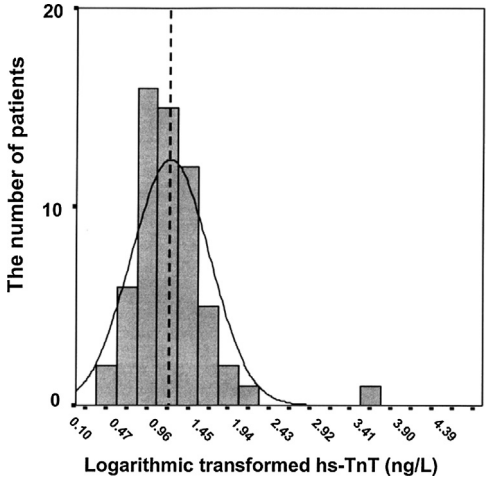

Fig. 1. Distribution of plasma high-sensitivity troponin T (hs-TnT). The figure shows distribution of plasma levels of hs-TnT (logarithmic transformed) of study population by histogram. Mean plasma hs-TnT was 0.110 ng/mL with standard deviation of 0.682 ng/mL and standard error of 0.088 ng/mL. Maximum and minimum values were 0.003 and 5.30 ng/mL, respectively. Median value of hs-TnT was 0.015 ng/mL. Dashed line shows the cutoff point determined by normal individuals (0.013 ng/mL).

Table 2
Simple correlation between hs-TnT and clinical parameters.

Variables	Correlation coefficient (r)	p-Value
Age (years)	−0.261	0.04
Aspartate aminotransferase (IU/L)	+0.266	0.04
hs-CRP (logarithmic transformed, ng/mL)	+0.280	0.03
eGFR (mL/min/1.73 m^2)	−0.560	<0.001
NT-pro BNP (logarithmic transformed, pg/mL)	+0.756	<0.001

hs-TnT, high-sensitivity troponin T; hs-CRP, high-sensitivity C reactive protein; eGFR, estimated glomerular filtration rate; NT-pro BNP, N-terminal pro-brain natriuretic peptide.

Table 3
Baseline characteristics of the patients divided by hs-TnT tertiles.

hs-TnT tertiles	T1 ($n = 16$)	T2 ($n = 24$)	T3 ($n = 20$)
Age (mean ± SD, years)	68.3 ± 8.5	69.7 ± 7.9	67.8 ± 12.3
Male patient (%)	9 (56.3)	10 (41.7)	11 (55.0)
Chest pain (%)	7 (43.4)	14 (58.3)	7(35.0)
Syncope (%)	3 (18.8)	6 (25.0)	2 (10.0)
Heart failure (%)	2 (13.1)	11 (45.8)*	10 (50.0)*
Body mass index (kg/m^2)	22.7 ± 0.8	23.7 ± 0.9	23.1 ± 0.7
Hypertension (%)	9 (56.3)	16 (66.7)	15 (75.0)
Dyslipidemia (%)	3 (18.8)	9 (37.5)	6 (30.0)
Diabetes mellitus (%)	3 (18.8)	8 (33.3)	6 (30.0)
Current smoker (%)	2 (12.5)	3 (12.5)	4 (20.0)
Peak-to-peak PG (mmHg)	83.3 ± 5.1	75.2 ± 5.7	87.1 ± 7.4
LVEDVI (mL/m^2)	83.7 ± 6.5	106.6 ± 10.8	98.5 ± 7.0
LVESVI (mL/m^2)	27.7 ± 1.9	43.4 ± 7.5	49.3 ± 6.9
LVEF (%)	66.8 ± 2.2	58.5 ± 3.0	56.4 ± 3.3
Aortic valve area (cm^2)	0.58 ± 0.05	0.67 ± 0.05	0.54 ± 0.05
The maximum PG (mmHg)	103.3 ± 4.9	95.7 ± 5.3	91.2 ± 5.1
The mean PG (mmHg)	61.9 ± 3.9	61.2 ± 4.5	54.3 ± 3.4
LVMI (g/m^2)	161.3 ± 15.2	180 ± 11.5	187 ± 16.8
hs-CRP (ng/mL)	1339 ± 676	1581 ± 729	3678 ± 1777
eGFR (mL/min/1.73 m^2)	76.1 ± 3.9	71.8 ± 2.7	55.7 ± 7.6*
hs-TnT (ng/mL)	0.007 ± 0.001	0.015 ± 0.001*	0.306 ± 0.263**

hs-TnT, high-sensitivity troponin T; SD, standard deviation; PG, pressure gradient through aortic valve; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate. T1, tertile 1; T2, tertile 2; T3, tertile 3.

* $p < 0.05$ versus T1.

** $p < 0.001$ versus T1, T2.

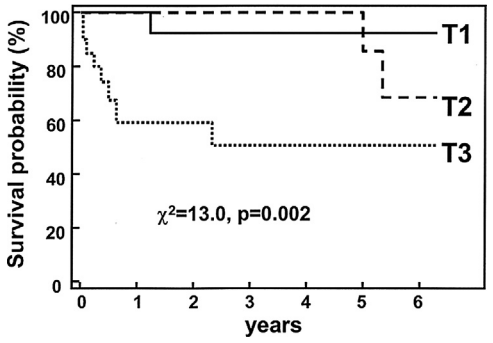

Fig. 2. Kaplan–Meier curve analysis of the primary endpoint. The figure shows the probability of surviving major adverse cardiovascular events (MACE) in groups of patients with aortic stenosis divided by tertiles of plasma high-sensitivity troponin T levels after aortic valve replacement surgery. Kaplan–Meier curve analysis revealed a statistically significant difference in the survival probability from the MACE among the three groups (log-rank test, $\chi^2 = 13.0$, $p = 0.002$). T1, tertile 1; T2, tertile 2; T3, tertile 3. Solid line, T1; dashed line, T2; broken line, T3.

Table 4
Summary of cardiovascular events in hs-TnT tertiles.

Event	T1	T2	T3
Re-admission due to congestive heart failure	0	1	0
Fatal arrhythmia	0	0	3
All cause death (cardiac death)	1 (1)	1 (0)	5 (4)
MACE	1	2	8

hs-TnT, high-sensitivity troponin T. Major adverse cardiovascular event (MACE) was defined as composite events of re-admission to the hospital for congestive heart failure, fatal arrhythmia, and all causes of death. T1, tertile 1; T2, tertile 2; T3, tertile 3.

Next, we analyzed the independent factors associated with MACE. A univariate Cox proportional hazard model analysis showed that eGFR and hs-TnT tertile were significant factors associated with MACE (Table 5). Then we performed a multivariable Cox analysis with the forced entry method, including the patients' demographic data and these variables (age, sex, eGFR, and hs-TnT tertile) as explanatory variables. We found that eGFR and hs-TnT tertile were independent factors for predicting MACE (Table 6).

We analyzed each cardiovascular event by Kaplan–Meier curve analysis. We found that the occurrence of fatal arrhythmia and cardiac death was significantly different among the three groups ($\chi^2 = 6.85$, $p = 0.03$ and $\chi^2 = 7.36$, $p = 0.03$, respectively). Fig. 3 shows the Kaplan–Meier curve analysis of arrhythmic events and cardiac death in the groups divided by hs-TnT tertile. A Cox proportional hazard analysis was not conducted because of the small number of the events.

One patient had cerebral bleeding and two patients complicated cerebral infarction, however all of these patients had already showed heart failure before the onset of stroke. Thus any thromboembolic events were not included in the present study.

Table 5
Results of Cox proportional hazard model analysis (univariate).

Variables	Hazard ratio (95% CI)	*p*-Value
Age	1.02 (0.95–1.09)	0.64
Male sex	0.78 (0.23–2.63)	0.69
Body mass index	0.92 (0.76–1.11)	0.37
Hypertension	1.36 (0.35–5.24)	0.65
Dyslipidemia	0.27 (0.03–2.01)	0.21
Diabetes mellitus	0.97 (0.26–3.66)	0.96
Smoking	1.38 (0.35–5.43)	0.65
LVEDVI (mL/m^2)	1.01 (0.99–1.03)	0.41
LVESVI (mL/m^2)	1.01 (0.99–1.03)	0.42
Maximum PG (mmHg)	1.00 (0.97–1.02)	0.74
Mean PG (mmHg)	1.00 (0.96–1.05)	0.90
AVA (cm^2)	0.03 (0.001–1.86)	0.10
Post operative maximum PG (mmHg)	0.97 (0.91–1.03)	0.97
Post operative LVEF (%)	0.98 (0.95–1.02)	0.90
Post operative AVA (cm^2)	0.04 (0.001–1.97)	0.11
LVMI (g/m^2)	1.00 (0.99–1.02)	0.68
LVEF (%)	0.98 (0.94–1.02)	0.34
hs-CRP (ng/mL)	1.22 (0.47–3.13)	0.68
eGFR (mL/min/1.73 m^2)	0.97 (0.95–0.99)	0.001
hs-TnT tertile	4.37 (1.53–12.5)	0.006

95% CI, 95% confidence interval; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; PG, pressure gradient through aortic valve; AVA, aortic valve area; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; hs-TnT: high-sensitivity troponin T. hs-CRP level was logarithmically transformed because of a non-parametric distribution.

Table 6
Results of Cox proportional hazard model analysis (multivariate).

Variables	Hazard ratio (95% CI)	*p*-Value
Age	1.01 (0.94–1.08)	0.90
Male sex	0.60 (0.17–2.14)	0.43
eGFR (mL/min/1.73 m^2)	0.98 (0.96–1.00)	0.04
hs-TnT tertile	3.71 (1.16–11.9)	0.03

95% CI, 95% confidence interval; eGFR, estimated glomerular filtration rate; hs-TnT, high-sensitivity troponin T.

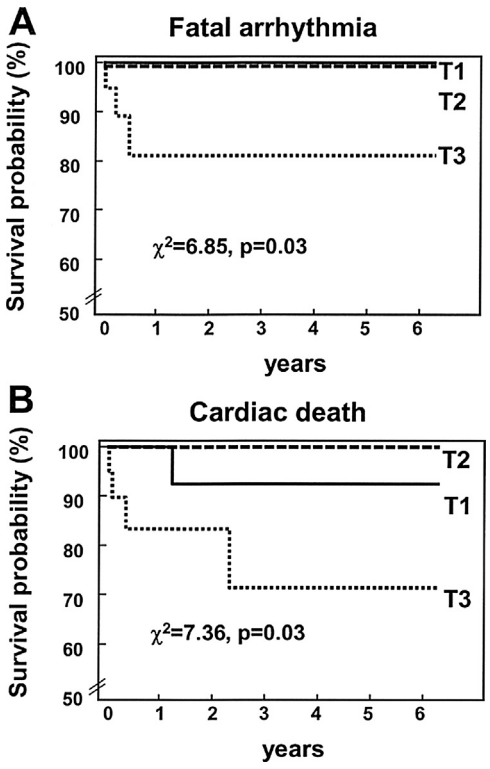

Fig. 3. Kaplan–Meier curve analysis of cardiovascular events. (A) Survival probability from fatal arrhythmia. The incidence of fatal arrhythmia was significantly different among the three groups divided by tertiles of plasma high-sensitivity troponin T levels after aortic valve replacement surgery ($\chi^2 = 6.85$, $p = 0.03$). (B) Survival probability from cardiac death. The incidence of cardiac death was significantly different among the three groups ($\chi^2 = 7.36$, $p = 0.03$). T1, tertile 1; T2, tertile 2; T3, tertile 3. Solid line, T1; dashed line, T2; broken line, T3.

Discussion

In this study we explored whether preoperative plasma cardiac troponin T levels were associated with MACE during the follow-up of severe AS patients who underwent AVR. The preoperative hs-TnT level was an independent predictor of MACE in patients with severe AS after the surgery. In particular, hs-TnT might be a predictor for the occurrence of fatal arrhythmia and cardiac death.

A recent high-sensitivity assay has shown that cardiac troponin levels were elevated in response to cardiovascular diseases and provide important prognostic information. The increased diagnostic and prognostic accuracy of the hs-TnT assay versus the conventional troponin T assay has recently been reported in several groups of patients with cardiovascular diseases such as subclinical cardiovascular diseases [16], heart failure [12], and acute [22] and stable [15] coronary artery diseases. Interestingly, hs-TnT levels were found to predict future heart failure in stable coronary artery disease [15]. The mechanisms responsible for the release of low levels of cardiac troponin T could include transient, clinically silent ischemic episodes and small-vessel occlusions; inflammatory processes; cardiomyocyte apoptosis; reduced renal clearance; and increased myocardial strain due to pressure or volume overload.

Stenosis of aortic valve increases pressure afterload and ventricular wall stress, resulting in pressure overload to the left ventricle. Indeed, the strong association between left ventricular mass and hs-TnT levels is also in line with experimental and clinical works showing the increased production of troponin T in human and rat myocardium during pressure overload [23]. The troponin elevation

seen with left ventricular hypertrophy (LVH) may be the result of myocardial ischemia due to a supply/demand mismatch in hypertrophied myocytes [24]. In our study, we found a significant positive correlation between plasma hs-TnT and NT-pro BNP, suggesting that hs-TnT is associated with cardiac overload.

One potential mechanism for increased MACE may be susceptibility for arrhythmia. Fibrosis can serve as a structural substrate for arrhythmia in patients with dilated cardiomyopathy and myocardial infarction has been linked to an increased incidence of arrhythmia and sudden cardiac death [25]. In patients with AS and concurrent LVH, fibrosis is also a common pathologic alteration [26]. Dweck et al. reported that myocardial fibrosis using late gadolinium enhancement (LGE) of cardiac magnetic resonance imaging (MRI) was related to prognostic significance in AS [27]. Similarly, LGE in cardiac MRI has been reported to predict cardiac events in hypertrophic cardiomyopathy [28]. These results suggest that the fibrosis of myocardium might involve arrhythmogenic substrates. The elevation of plasma troponin T levels might reflect the micro-ischemia and degradation of cardiac myocytes and progression of myocardial fibrosis. Similar to hs-TnT, circulating tenascin C has been reported to predict heart failure in patients with hypertrophic cardiomyopathy [29]. The development of these specific biomarkers for cardiovascular disease is needed for prevention of major adverse events.

Røsjø et al. reported that hs-TnT could be a marker to predict the prognosis of AS in 57 patients [30]. They observed 30 patients (53%) patients who underwent AVR surgery and the natural course in the remaining 27 patients. In our study, all of the subjects underwent AVR and we clearly demonstrated that the hs-TnT could be a prognostic marker after AVR in patients with severe AS. Together with hs-TnT, eGFR was an independent factor to predict MACE in patients with AS. Although plasma levels of troponin T increase in patients with renal failure, we found that these two parameters were independently associated with cardiovascular events in AS patients. Precisely how these parameters are associated with cardiac events after AVR should be elucidated.

In conclusion, preoperative plasma hs-TnT levels could be a novel biomarker for predicting MACE in patients with severe AS post-AVR. Further study is needed to clarify the precise role of hs-TnT in the pathology of severe AS.

Study limitations

Our study has several limitations. First, we measured the level of hs-TnT before AVR. It might be useful to follow the changes in plasma hs-TnT levels after AVR to provide more information about the relation between hs-TnT and MACE in severe AS patients. Second, our study had a relatively small number of patients and was a single-center study. However, a single-center study guarantees the essential uniformity in patient selection, surgical techniques, and postoperative care. Third, the incidence of bicuspid aortic valves was over half of the total subjects. We still do not know the reason. Because the etiology of AS might affect the clinical outcome, this point should be taken into account for the interpretation of our data. Further study is needed with a larger population to confirm the significance of hs-TnT in these events.

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